

Application Serial No.: 09/914,605

IN THE CLAIMS:

1-105. Canceled

106. (Currently amended) A delivery vehicle for use in targeted delivery of an active agent, the delivery vehicle comprising a targeting agent and a pharmaceutically acceptable diluent or excipient, wherein the targeting agent that preferentially binds a radiation inducible target in a target tissue.

107. (Original) The delivery vehicle of claim 106, wherein the targeting agent preferentially binds an activated platelet.

108. (Original) The delivery vehicle of claim 106, wherein the targeting agent is selected from the group consisting of a protein; a peptide; an antibody; a genetic construct; and combinations thereof.

109. (Currently amended) ~~The~~ A delivery vehicle for use in targeted delivery of an active agent, the delivery vehicle comprising a targeting agent and a pharmaceutically acceptable diluent or excipient, wherein the targeting agent preferentially binds a radiation inducible target in a target tissue and comprises ~~delivery vehicle of claim 108, wherein the protein is fibrinogen or a peptide fragment or analog thereof.~~

110. (Original) The delivery vehicle of claim 109, wherein the peptide fragment of fibrinogen is a gamma subunit peptide fragment of fibrinogen.

111. (Original) The delivery vehicle of claim 110, wherein the gamma subunit peptide fragment of fibrinogen comprises any of SEQ ID NOs:1-10, or comprises an analog or fragment of any of SEQ ID NOs:1-10.

112. (Original) The delivery vehicle of claim 111, wherein the gamma subunit peptide fragment of fibrinogen comprises HHLGGAKQAGDV (SEQ ID NO:1).

113. (Original) The delivery vehicle of claim 106, further comprising an active agent.

114. (Original) The delivery vehicle of claim 113, wherein the active agent comprises an imaging agent.

Application Serial No.: 09/914,605

115. (Original) The delivery vehicle of claim 114, wherein the imaging agent is selected from the group consisting of paramagnetic, radioactive and fluorogenic ions.

116. (Original) The delivery vehicle of claim 115, wherein the radioactive imaging agent is selected from the group consisting of gamma-emitters, positron-emitters and x-ray-emitters.

117. (Original) The delivery vehicle of claim 114, wherein the radioactive imaging agent is selected from the group consisting of ^{43}K , ^{52}Fe , ^{57}Co , ^{67}Cu , ^{67}Ga , ^{68}Ga , ^{77}Br , ^{81}Rb , $^{81\text{M}}\text{Kr}$, $^{87\text{M}}\text{Sr}$, $^{99\text{M}}\text{Tc}$, ^{111}In , ^{113}In , ^{123}I , ^{125}I , ^{127}Cs , ^{129}Cs , ^{131}I , ^{132}I , ^{197}Hg , ^{203}Pb and ^{208}Bi .

118. (Currently amended) The delivery vehicle of claim 114, wherein the radioactive imaging agent is present in the ~~platelet~~ delivery vehicle in an amount ranging from about 0.1 to about 100 millicuries.

119. (Currently amended) The delivery vehicle of claim 118, wherein the radioactive imaging agent is present in the ~~platelet~~ delivery vehicle in an amount ranging from about 1 to about 10 millicuries.

120. (Currently amended) The delivery vehicle of claim 119, wherein the radioactive imaging agent is present in the ~~platelet~~ delivery vehicle in an amount ranging from about 2 to about 5 millicuries.

121. (Currently amended) The delivery vehicle of claim 120, wherein the radioactive imaging agent is present in the ~~platelet~~ delivery vehicle in an amount ranging from about 1 to about 5 millicuries.

122. (Original) The delivery vehicle of claim 113, wherein the active agent comprises a therapeutic agent.

123. (Original) The delivery vehicle of claim 122, wherein the therapeutic agent is selected from the group consisting of a chemotherapeutic agent, a toxin, a radiotherapeutic agent, a radiosensitizing agent and combinations thereof.

124. (Original) The delivery vehicle of claim 123, wherein the chemotherapeutic agent is selected from the group consisting of an anti-tumor drug,

Application Serial No.: 09/914,605

a cytokine, an anti-metabolite, an alkylating agent, a hormone, methotrexate, doxorubicin, daunorubicin, cytosine arabinoside, etoposide, 5-4 fluorouracil, melphalan, chlorambucil, a nitrogen mustard, cyclophosphamide, *cis*-platinum, vindesine, vinca alkaloids, mitomycin, bleomycin, purothionin, macromomycin, 1,4-benzoquinone derivatives, trenimon, steroids, aminopterin, anthracyclines, demecolcine, etoposide, mithramycin, doxorubicin, daunomycin, vinblastine, neocarzinostatin, macromycin, α -amanitin, and combinations thereof.

125. (Original) The delivery vehicle of claim 123, wherein the toxin is selected from the group consisting of Russell's Viper Venom, activated Factor IX, activated Factor X, thrombin, phospholipase C, cobra venom factor, ricin, ricin A chain, *Pseudomonas* exotoxin, diphtheria toxin, bovine pancreatic ribonuclease, pokeweed antiviral protein, abrin, abrin A chain, gelonin, saporin, modeccin, viscumin, volkensin and combinations thereof.

126. (Original) The delivery vehicle of claim 123, wherein the radiotherapeutic agent is selected from the ^{47}Sc , ^{67}Cu , ^{90}Y , ^{109}Pd , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{199}Au , ^{211}At , ^{212}Pb , ^{212}Bi , ^{32}P , ^{33}P , ^{71}Ge , ^{77}As , ^{103}Pb , ^{105}Rh , ^{111}Ag , ^{119}Sb , ^{121}Sn , ^{131}Cs , ^{143}Pr , ^{161}Tb , ^{177}Lu , ^{191}Os , $^{193\text{M}}\text{Pt}$, and ^{197}Hg .

127. (Original) The delivery vehicle of claim 123, wherein the radiosensitizing agent is selected from the group consisting of an anti-angiogenic agent; a DNA protein kinase inhibitor; a tyrosine kinase inhibitor; a DNA repair enzyme inhibitor; nitroimidazole; metronidazole; misonidazole; a genetic construct comprising an enhancer-promoter region which is responsive to radiation, and at least one structural gene whose expression is controlled by the enhancer-promoter; boron-neutron capture reagents; and combinations thereof.

128. (Original) The delivery vehicle of claim 127, wherein the genetic construct further comprises a viral vector.

129. (Original) The delivery vehicle of claim 123, wherein the therapeutic agent is a chemotherapeutic agent, and the delivery vehicle comprising the

Application Serial No.: 09/914,605

chemotherapeutic agent is administered in an amount ranging from about 10 to about 1000 mg.

130. (Original) The delivery vehicle of claim 129, wherein the delivery vehicle comprising the chemotherapeutic agent is administered in an amount ranging from about 50 to about 500 mg.

131. (Original) The delivery vehicle of claim 130, wherein the delivery vehicle comprising the chemotherapeutic agent is administered in an amount ranging from about 100 to about 250 mg.

132. (Original) The delivery vehicle of claim 123, wherein the therapeutic agent is a toxin, and the delivery vehicle comprising the toxin is administered in an amount ranging from about 1 to about 500 μ g.

133. (Original) The delivery vehicle of claim 132, wherein the delivery vehicle comprising the toxin is administered in an amount ranging from about 10 to about 100 μ g.

134. (Original) The delivery vehicle of claim 133, wherein the delivery vehicle comprising the toxin is administered in an amount ranging from about 20 to 50 μ g.

135. (Original) The delivery vehicle of claim 134, wherein the therapeutic agent is a radiotherapeutic agent, and the delivery vehicle comprising the radiotherapeutic agent is administered in an amount ranging from about 0.5 to about 100 mg.

136. (Original) The delivery vehicle of claim 135, wherein the delivery vehicle comprising the radiotherapeutic agent is administered in an amount ranging from about 1 to about 50 mg.

137. (Original) The delivery vehicle of claim 136, wherein the delivery vehicle comprising the radiotherapeutic agent is administered in an amount ranging from about 5 to about 10 mg.

138. (Currently amended) ~~The delivery vehicle of claim 106,~~ A delivery vehicle for use in targeted delivery of an active agent, the delivery vehicle comprising a targeting agent and a pharmaceutically acceptable diluent or excipient, wherein the

Application Serial No.: 09/914,605

~~targeting agent that preferentially binds a radiation inducible target wherein the radiation-inducible target~~ is selected from the group consisting of ICAM-1, E-selectin, P-selectin, β_3 Integrin, and combinations thereof.

139. (Currently amended) The delivery vehicle of claim [[106]] 138, further comprising a carrier.

140. (Currently amended) The delivery vehicle of claim 139, wherein the carrier and the targeting agent are the same.

141. (Original) The delivery vehicle of claim 139, wherein the carrier is selected from the group consisting of a platelet; a leukocyte; a protein; a peptide; an antibody; a microsphere; a liposome; a genetic construct; and combinations thereof.

142. (Currently amended) A delivery vehicle for use in targeted delivery of an active agent, the delivery vehicle comprising:

- (a) a liposome carrier; ~~and~~
- (b) a targeting agent that preferentially binds a radiation inducible target; and
- (c) a pharmaceutically acceptable diluent or excipient.

143. (Original) The delivery vehicle of claim 142, wherein the liposome carrier further comprises a lipid selected from the group consisting of phosphatidylcholines (lecithins) (PC), phosphatidylethanolamines (PE), lysolecithins, lysophosphatidylethanolamines, phosphatidylserines (PS), phosphatidylglycerols (PG), phosphatidylinositol (PI), sphingomyelins, cardiolipin, phosphatidic acids (PA), fatty acids, gangliosides, glucolipids, glycolipids, mono-, di or triglycerides, ceramides, cerebroside and combinations thereof.

144. (Original) The delivery vehicle of claim 143, wherein the liposome carrier further comprises a cationic lipid selected from the group consisting of 1,2-dioleoyloxy-3-(trimethylamino) propane (DOTAP); N-[1-(2,3,-ditetradecyloxy)propyl]-N,N-dimethyl-N-hydroxyethylammonium bromide (DMRIE); N-[1-(2,3,-dioleoyloxy)propyl]-N,N-dimethyl-N-hydroxy ethylammonium bromide (DORIE); N-[1-(2,3-dioleoyloxy) propyl]-N,N,N-trimethylammonium chloride (DOTMA); 3β [N-(N',N'-

Application Serial No.: 09/914,605

dimethylaminoethane)carbamoyle] cholesterol (DC-Chol); and dimethyldioctadecylammonium (DDAB); dioleoylphosphatidyl ethanolamine (DOPE), cholesterol-containing DOPC, and combinations thereof.

145. (Original) The delivery vehicle of claim 142, wherein the liposome further comprises a hydrophilic polymer coating and the hydrophilic polymer is selected from the group consisting of polyvinylpyrrolidone, polyvinylmethylether, polymethyloxazoline, polyethyloxazoline, polyhydroxypropyloxazoline, polyhydroxypropylmethacrylamide, polymethacrylamide, polydimethylacrylamide, polyhydroxypropylmethacrylate, polyhydroxyethylacrylate, hydroxymethylcellulose, hydroxyethylcellulose, polyethyleneglycol, polyaspartamide and combinations thereof.

146. (Original) The delivery vehicle of claim 142, wherein the targeting agent preferentially binds an activated platelet.

147. (Original) The delivery vehicle of claim 142, wherein the targeting agent is selected from the group consisting of a protein; a peptide; an antibody; a genetic construct; and combinations thereof.

148. (Currently amended) ~~The delivery vehicle of claim 147, A delivery vehicle for use in targeted delivery of an active agent, the delivery vehicle comprising:~~

(a) a liposome carrier;

(b) a targeting agent that preferentially binds a radiation inducible target,
wherein the ~~protein~~ targeting agent is fibrinogen or a peptide fragment or analog thereof; and

(c) a pharmaceutically acceptable diluent or excipient .

149. (Original) The delivery vehicle of claim 148, wherein the peptide fragment of fibrinogen is a gamma subunit peptide fragment of fibrinogen.

150. (Original) The delivery vehicle of claim 149, wherein the gamma subunit peptide fragment of fibrinogen comprises any of SEQ ID NOs:1-10, or comprises an analog or fragment of any of SEQ ID NOs:1-10.

Application Serial No.: 09/914,605

151. (Original) The delivery vehicle of claim 150, wherein the gamma subunit peptide fragment of fibrinogen comprises HHLGGAKQAGDV (SEQ ID NO:1).

152. (Original) The delivery vehicle of claim 142, further comprising an active agent.

Please add the following new claims:

153. (New) The delivery vehicle of claim 106, wherein the radiation inducible target is selected from the group consisting of ICAM-1, E-selectin, P-selectin, β_3 integrin, an activated platelet, and combinations thereof.

154. (New) The delivery vehicle of claim 106, wherein the radiation inducible target is a cell adhesion molecule.

155. (New) The delivery vehicle of claim 138, wherein the targeting agent is selected from the group consisting of a protein; a peptide; an antibody; a genetic construct; and combinations thereof.

156. (New) The delivery vehicle of claim 155, wherein the targeting agent is an antibody or a derivative thereof, wherein the antibody or derivative thereof preferentially binds a radiation inducible target selected from the group consisting of ICAM-1, E-selectin, P-selectin, β_3 integrin, and combinations thereof.

157. (New) The delivery vehicle of claim 156, wherein the antibody derivative is selected from the group consisting of an intact immunoglobulin molecule, a single chain immunoglobulin molecule, an Fab fragment, an Fab' fragment, an F(ab')₂ fragment, an F(v) fragment, a single-chain Fv antibody (scFv), a humanized antibody, and a monoclonal antibody.

158. (New) The delivery vehicle of claim 138, further comprising an active agent.

159. (New) The delivery vehicle of claim 158, wherein the active agent comprises an imaging agent.

160. (New) The delivery vehicle of claim 159, wherein the imaging agent is selected from the group consisting of paramagnetic, radioactive and fluorogenic ions.

Application Serial No.: 09/914,605

161. (New) The delivery vehicle of claim 160, wherein the radioactive imaging agent is selected from the group consisting of gamma-emitters, positron-emitters and x-ray-emitters.

162. (New) The delivery vehicle of claim 159, wherein the radioactive imaging agent is selected from the group consisting of ^{43}K , ^{52}Fe , ^{57}Co , ^{67}Cu , ^{67}Ga , ^{68}Ga , ^{77}Br , ^{81}Rb , $^{81\text{M}}\text{Kr}$, $^{87\text{M}}\text{Sr}$, $^{99\text{M}}\text{Tc}$, ^{111}In , ^{113}In , ^{123}I , ^{125}I , ^{127}Cs , ^{129}Cs , ^{131}I , ^{132}I , ^{197}Hg , ^{203}Pb and ^{206}Bi .

163. (New) The delivery vehicle of claim 159, wherein the radioactive imaging agent is present in the delivery vehicle in an amount ranging from about 0.1 to about 100 millicuries.

164. (New) The delivery vehicle of claim 163, wherein the radioactive imaging agent is present in the delivery vehicle in an amount ranging from about 1 to about 10 millicuries.

165. (New) The delivery vehicle of claim 164, wherein the radioactive imaging agent is present in the delivery vehicle in an amount ranging from about 2 to about 5 millicuries.

166. (New) The delivery vehicle of claim 165, wherein the radioactive imaging agent is present in the delivery vehicle in an amount ranging from about 1 to about 5 millicuries.

167. (New) The delivery vehicle of claim 158, wherein the active agent comprises a therapeutic agent.

168. (New) The delivery vehicle of claim 167, wherein the therapeutic agent is selected from the group consisting of a chemotherapeutic agent, a toxin, a radiotherapeutic agent, a radiosensitizing agent and combinations thereof.

169. (New) The delivery vehicle of claim 168, wherein the chemotherapeutic agent is selected from the group consisting of an anti-tumor drug, a cytokine, an anti-metabolite, an alkylating agent, a hormone, methotrexate, doxorubicin, daunorubicin, cytosine arabinoside, etoposide, 5-fluorouracil, melphalan, chlorambucil, a nitrogen mustard, cyclophosphamide, *cis*-platinum, vindesine, vinca alkaloids, mitomycin,

Application Serial No.: 09/914,605

bleomycin, purothionin, macromomycin, 1,4-benzoquinone derivatives, trenimon, steroids, aminopterin, anthracyclines, demecolcine, etoposide, mithramycin, doxorubicin, daunomycin, vinblastine, neocarzinostatin, macromycin, α -amanitin, and combinations thereof.

170. (New) The delivery vehicle of claim 168, wherein the toxin is selected from the group consisting of Russell's Viper Venom, activated Factor IX, activated Factor X, thrombin, phospholipase C, cobra venom factor, ricin, ricin A chain, *Pseudomonas* exotoxin, diphtheria toxin, bovine pancreatic ribonuclease, pokeweed antiviral protein, abrin, abrin A chain, gelonin, saporin, modeccin, viscumin, volkensin and combinations thereof.

171. (New) The delivery vehicle of claim 168, wherein the radiotherapeutic agent is selected from the group consisting of ^{47}Sc , ^{67}Cu , ^{90}Y , ^{109}Pd , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{199}Au , ^{211}At , ^{212}Pb , ^{212}Bi , ^{32}P , ^{33}P , ^{71}Ge , ^{77}As , ^{103}Pb , ^{105}Rh , ^{111}Ag , ^{119}Sb , ^{121}Sn , ^{131}Cs , ^{143}Pr , ^{161}Tb , ^{177}Lu , ^{191}Os , $^{193\text{M}}\text{Pt}$, and ^{197}Hg .

172. (New) The delivery vehicle of claim 168, wherein the radiosensitizing agent is selected from the group consisting of an anti-angiogenic agent; a DNA protein kinase inhibitor; a tyrosine kinase inhibitor; a DNA repair enzyme inhibitor; nitroimidazole; metronidazole; misonidazole; a genetic construct comprising an enhancer-promoter region which is responsive to radiation, and at least one structural gene whose expression is controlled by the enhancer-promoter; boron-neutron capture reagents; and combinations thereof.

173. (New) The delivery vehicle of claim 172, wherein the genetic construct further comprises a viral vector.

174. (New) The delivery vehicle of claim 168, wherein the therapeutic agent is a chemotherapeutic agent, and the delivery vehicle comprising the chemotherapeutic agent is administered in an amount ranging from about 10 to about 1000 mg.

Application Serial No.: 09/914,605

175. (New) The delivery vehicle of claim 174, wherein the delivery vehicle comprising the chemotherapeutic agent is administered in an amount ranging from about 50 to about 500 mg.

176. (New) The delivery vehicle of claim 175, wherein the delivery vehicle comprising the chemotherapeutic agent is administered in an amount ranging from about 100 to about 250 mg.

177. (New) The delivery vehicle of claim 168, wherein the therapeutic agent is a toxin, and the delivery vehicle comprising the toxin is administered in an amount ranging from about 1 to about 500 μ g.

178. (New) The delivery vehicle of claim 177, wherein the delivery vehicle comprising the toxin is administered in an amount ranging from about 10 to about 100 μ g.

179. (New) The delivery vehicle of claim 178, wherein the delivery vehicle comprising the toxin is administered in an amount ranging from about 20 to 50 μ g.

180. (New) The delivery vehicle of claim 179, wherein the therapeutic agent is a radiotherapeutic agent, and the delivery vehicle comprising the radiotherapeutic agent is administered in an amount ranging from about 0.5 to about 100 mg.

181. (New) The delivery vehicle of claim 180, wherein the delivery vehicle comprising the radiotherapeutic agent is administered in an amount ranging from about 1 to about 50 mg.

182. (New) The delivery vehicle of claim 181, wherein the delivery vehicle comprising the radiotherapeutic agent is administered in an amount ranging from about 5 to about 10 mg.

183. (New) The delivery vehicle of claim 142, wherein the radiation inducible target is selected from the group consisting of ICAM-1, E-selectin, P-selectin, β_3 integrin, an activated platelet, and combinations thereof.

184. (New) The delivery vehicle of claim 142, wherein the radiation inducible target is a cell adhesion molecule.